Time trends and pathological profile of carcinoma lower oesophagus and gastro-oesophageal junction over the last 20 years - an experience from South India

JOSE TONY, SUNIL KUMAR K, VARGHESE THOMAS

ABSTRACT

There is an upward trend in the incidence of adenocarcinoma lower oesophagus in western countries. However there is only limited comparable data from Asian countries. We conducted a retrospective analysis of our data compiled over a twenty-year period (1985–2004). All lesions diagnosed as either squamous cell carcinoma or adenocarcinoma involving the oesophagus with or without involvement of the gastro-oesophageal junction were included in the study. 476 cases with biopsy proven malignancy (either adeno or squamous) of lower oesophagus were studied. The pattern of change in frequency and histology over twenty years was analysed using the chi square test for trend. There was a consistent increase in the frequency of cancer involving the gastro-oesophageal junction though it did not reach statistical significance (p =0.15). Out of 476 lower oesophageal cancers, 249 were adeno-carcinomas and 227 were squamous cell carcinomas. Adenocarcinoma involving the gastro-oesophageal junction showed consistent increase even though the p value was not significant (p =0.09) and this therefore requires further longitudinal studies. There was no change in trend for pattern and frequency of squamous cell carcinoma oesophagus involving different sub-sites during the study period.

Key words: oesophagus, carcinoma, gastro-oesophageal junction, time trends.

INTRODUCTION

The common types of oesophageal carcinoma are squamous cell carcinoma (SCC) and adenocarcinoma (AC). SCC predominantly involves the upper and middle oesophagus whilst adenocarcinoma mainly affects the lower oesophagus and/or the gastro-oesophageal junction. Over the last three decades, adenocarcinoma oesophagus has overtaken SCC as the predominant histologic type in the western world.[1, 2, 3] In developing countries, SCC is the most common histologic type.[4,5,6]

Studies concerning the incidence of cancer show an overall decline in SCC since the early 1970s in the western world.[7,8] But the incidence of oesophageal adenocarcinoma has shown a remarkable increase during the last three decades in the United States and Europe.[2,3] Only few time trend studies are available from Asian countries.[9] Chang et al from Taiwan have reported an unchanged incidence of adenocarcinoma lower oesophagus and gastric cardia over 15 years.[10] There are no Indian studies addressing time trends in the occurrence of oesophageal carcinoma. Therefore we tried to assess the frequency trend of sub-site involvement and histology of carcinoma oesophagus including gastro-oesophageal junction cancers over a twenty year period.

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METHODS

This retrospective study was conducted in the Department of Gastroenterology at Calicut Medical College by the careful scrutiny of endoscopy and biopsy registers from January 1985 to December 2004. A descriptive and uniform endoscopy report format illustrating the site and extent of lesions has been maintained in the department since 1982. Endoscopy registers were searched for reports of suspicious malignancy involving the oesophagus and gastro-oesophageal junction and these were selected for this study.

Endoscopically the oesophagus was arbitrarily divided into three parts; upper oesophagus-16 to 24 cm from the incisors, middle oesophagus-24 to 32 cm, lower oesophagus-32 cm until the gastro-oesophageal junction. The gastro-oesophageal junction where visible was defined as the endoscopically visualised point of the proximal end of the gastric folds. The cardia was defined as an area of stomach approximately 3 cm below the level of the gastro-oesophageal junction. The location of neoplasm in the oesophagus was noted with reference to the markings on the endoscope. Neoplasms of the lower third of the oesophagus were divided into two groups: Group A lesions involving the lower oesophagus and the gastro-oesophageal junction; and Group B lesions not involving the gastro-oesophageal junction. If the endoscope could not be negotiated beyond the lesion, the extent of longitudinal growth was ascertained from barium swallow or CT scan reports if available. In the case of gastro-oesophageal junction cancers, involvement of the stomach was ascertained from the case records (evidence from barium study, CT scan or operative findings) and if this was not possible, those cases were excluded from the study. If the growth was seen to extend through two or more sub-sites, the region with maximum extent was taken as the dominant site of cancer. Only cases of malignancy with either adeno or squamous cell carcinoma were enrolled in the study. All other histologic types and cases with inconclusive biopsy reports were also excluded.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS for Windows version 11.0. Cancer occurrence trend over this time period for lesions involving the lower oesophagus and the gastro-oesophageal junction (Group A) and lower oesophagus alone (Group B) were tested using the chi square test for time trend. Percentages of histologic subtypes in each group were calculated and the trend in pattern and frequency of histology

over this period was tested using the chi square test for trend. P value of less than 0.05 was considered significant.

RESULTS

Among 29,926 upper GI endoscopies performed over 20 years, 909 cases of oesophageal neoplasm were identified. 51 (5.6%) cases were excluded from the present analysis for the following reasons; inconclusive biopsy report (21 cases), inability to asses the gastric extent of gastro-oesophageal junction lesions (25 cases) and histology other than AC or SCC (5 cases). Selected cases were divided into five four-year groups: 1985–88, 1989–92, 1993–96, 1997–2000 and 2001–04.

After satisfying the inclusion and exclusion criteria, 858 cases were selected for final analysis. Mean age of the study population was 63.12 ±11.2 years (range 28–87). Male: female ratio was 2.77:1. Malignancy in the upper, middle and lower thirds of the oesophagus were seen in 41 (4.7%), 341 (39.7%) and 476 (55.4%) cases respectively. All neoplasms affecting the upper and the middle thirds were squamous in nature. Of the 476 carcinoma lower oesophagus cases, 249 (52.3%) were adenocarcinomas and 227(47.7%) were squamous cell carcinomas. Squamous cell carcinoma was the predominant histologic type (71%) of oesophageal cancer whereas adenocarcinoma constituted only 29% of cases in our study.

Among the 476 malignancy cases of the lower third of oesophagus, 336 (70.59%) cases could be included in group A and 140 (29.41%) patients in group B. The demographic details and frequency distribution of neoplasm during each four-year period for both groups is given in Table I. Cancer frequency trend during this period was tested using the chi square test for time trend and the trend curve is shown in figure I. There was consistent increase in the frequency of cancer in group A, however the analysis for trend did not reach statistical significance (p =0.15). But in group B, the trend curve was irregular and statistical analysis for trend was not significant (p=0.77)

In group A patients with lesions extending to the gastro-oesophageal junction, AC was the predominant histologic type of cancer which constituted 68.4% of cases (230 out of 336). In group B patients with lower end lesions not extending to the gastro-oesophageal junction, SCC was the predominant histologic type in 86.4% (121 out of 140) and adenocarcinoma was seen only in 13.5% (19/140) of cases. Frequency distribution for the histologic type of neoplasm in both groups A and B over each four-year period is given in Table II. Trend for frequency of adenocarcinoma and squamous cell carcinoma in both groups during the study period was tested and the trend curve is shown in figure II. There was consistent increase in the frequency of adenocarcinoma in group A but it did not reach statistical significance (p =0.09). There was no change in trend for frequency of SCC in both groups over twenty years (p = 0.88 and 0.93 respectively for groups A and B). The trend in the proportion of both histologic types in groups A and B was also assessed (Table III and Figure III) and no change was seen[p = 0.86 (group A) and p= 0.76 (group B)]

Table I: Demographic details and frequency distribution of neoplasia during the each four year period in group A and B

	Group A (n=336)	Group B (n=140)
Mean age (yrs)	64.18 ±11.41	62.41±10.56
Male: Female ratio	2.62 :1	2.91 : 1
Frequency in each four year period (number)		
1985–1988	55	28
1989–1992	64	29
1993–1996	68	23
1997–2000	71	30
2001–2004	78	30

DISCUSSION

In western countries, the incidence of SCC oesophagus is progressively decreasing, but the incidence of adenocarcinoma has shown dramatic increase.[2,7] There is wide geographic variation in the prevalence of SCC which is very common in

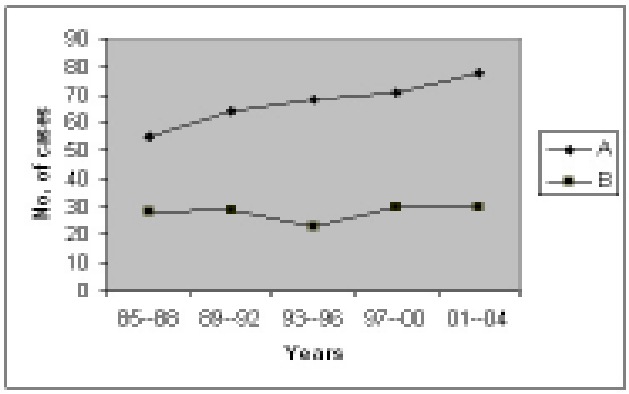

Fig. 1: Frequency distribution of neoplasia during the each four year period in group A and B. A-lesions involving lower oesophagus and gastro-oesophageal junction, B-lesions involving lower oesophagus alone without involvement of gastro-oesophageal junction

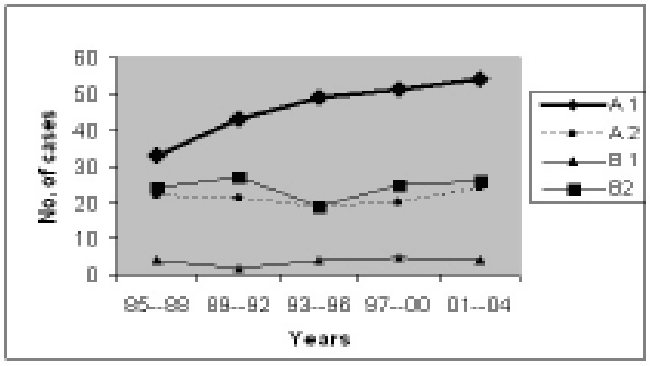

Fig. 2: Frequency distribution of AC and SC in both groups over each four year period. A1–AC at lower oesophagus and gastro-oesophageal junction, A2–SC at lower oesophagus and gastro-oesophageal junction, B1–AC at lower oesophagus alone without involvement of gastro-oesophageal junction, B2–SC at lower oesophagus alone without involvement of gastro-oesophageal junction

Table II: Frequency distribution of adeno carcinoma and squamous carcinoma in both groups over each four year period (number and percentage)

	Adenocarcinoma			Squamous carcinoma		
	Total	Group A	Group B	Total	Group A	Group B
1985–1988	38	34(89.5%)	4(10.5%)	46	22(47.8%)	24(52.2%)
1989 –1992	45	43(95.5%)	2(4.5%)	48	21(43.75%)	27(56.25%)
1993–1996	53	49(92.5%)	4(7.5%)	38	19(50%)	19(50%)
1997–2000	57	52(91.2%)	5(8.8%)	44	19(43.2%)	25(56.8%)
2001–2004	57	53(93%)	4(7%)	51	25(49%)	26(51%)

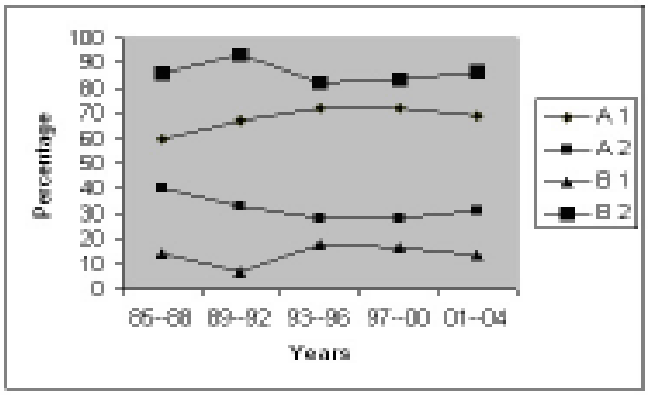

Fig. 3: Proportion (pattern) of AC and SC at both subsites over each four year period. A1–AC at lower oesophagus and gastro-oesophageal junction, A2–SC at lower oesophagus and gastro-oesophageal junction, B1–AC at lower oesophagus alone without involvement of gastro-oesophageal junction, B2–SC at lower oesophagus alone without involvement of gastro-oesophageal junction

Table III: Proportion of adenocarcinoma and squamous carcinoma at both subsites over each four year peiod

	Group A			Group B		
	Total	AC	SC	Total	AC	SC
1985–1988	55	33(60%)	22(40%)	28	4(14.3%)	24(85.7%)
1989–1992	64	43(67.2%)	21(32.8%)	29	2(6.9%)	27(93.1%)
1993–1996	68	49(72%)	19(28%)	23	4(17.4%)	19(82.6%)
1997–2000	71	51(72%)	20(28%)	30	5(16.67%)	25(83.3%)
2001–2004	78	54(70%)	24(30%)	30	4(13.3%)	(86.67%)

Asia, Africa and Iran.[11] A study from Pakistan reported that SCC was the predominant form of oesophageal carcinoma and 60% of these malignancies were located in the lower third.[12] Ansari et al, from North India had shown that 80% of oesophageal neoplasm were of the squamous type.[13] Mehrotra et al, reported that the middle third of the oesophagus was the most common site of oesophageal cancer in India and more than 95% of neoplasms were of the SCC type.[5] In a report from Mumbai, 50% of oesophageal cancers were located in the middle third, 30% in the lower third and 15% in the upper third of the oesophagus. 90% of these cancers were of the squamous cell type and only 10% were adenocarcinomas.[14]

In our study, 55% of neoplasms affected the lower third of the oesophagus and gastro-oesophageal junction which is comparable to the recent study from Quetta in Pakistan.[12] About 40% of neoplasms in our study were located in the middle third and only 5% were located in the upper third. In our study, SCC was the predominant histologic type of oesophageal cancer (71%). The middle third of the oesophagus was the most common site for SCC. Even though AC contributed to only 29% of all oesophageal cancers, there was significantly more AC in the lower end than SCC. This pattern is similar to that seen in many western studies which depict a higher prevalence for adenocarcinoma in the lower third.[2,3] In our study, AC constituted only 13.6% of cancers of lower third oesophagus not involving the gastro-oesophageal junction. A previous study has shown that only 9% of lower end neoplasms not involving the gastro-oesophageal junction were of the adenocarcinoma type.[15]

Chronic acid reflux into the oesophagus is considered a risk factor of adenocarcinoma gastro-oesophageal junction and lower oesophagus. Two large population-based studies have shown that chronic reflux is associated with increased risk of adenocarcinoma lower oesophagus and cardia.[16,17] But, in another population-based study from Denmark, more than 50% of patients with oesophageal adenocarcinoma had no history of symptomatic reflux disease.[18] A report from Malaysia has shown that Indian ethnicity was significantly associated with endoscopic oesophagitis and Barrett's metaplasia.[19] There are reports showing increasing frequency of reflux disease in the Asian population, though not as high as in the western population.[20,21]

Increasing prevalence of reflux disease in the Asian region may be one factor behind the high frequency of adenocarcinoma gastro-oesophageal junction and lower oesophagus in our study population. But, this alone may not explain the high frequency of adenocarcinoma. There may be a high prevalence of asymptomatic reflux which may also contribute to the development of AC as explained in a previous study by Bytzer et al.[18] Another contributing factor may be the difficulty in defining gastro-oesophageal junction neoplasms. In many cases, the exact localisation of neoplasm origin is not possible because a true oesophageal growth may extend downwards through the gastro-oesophageal junction and growths from the cardia and fundus may extend upwards into the oesophagus. According to Siewert's classification of neoplasms of the gastro-oesophageal junction, those lesions arising from the cardia and subcardia of the stomach are also included among gastro-oesophageal junction neoplasms.[22]

Hence the inclusion of neoplasms arising from the cardia may be another factor behind the high frequency of lower end neoplasms especially AC reported in western literature.

The changing epidemiology of oesophageal carcinoma may be a factor behind this trend of increase in lower end cancer rate. High consumption of smoked fish was a risk factor for oesophageal carcinoma in a study from Calicut.[23] Increasing alcohol consumption in the state of Kerala may be another factor behind this increase. Rao et al had shown that increasing alcohol consumption was a risk factor for oesophageal cancer.[24]

Time trend of frequency of neoplasms involving the gastro-oesophageal junction, especially the adenocarcinoma showed a consistent rise in our study population even though it was not statistically significant. Studies from the western world

and one study from our own institute have shown that neoplasms of the cardia have an increasing trend.[25,26] But in our study there was no change in time trend for neoplasms arising from the lower end of the oesophagus without involving the gastro-oesophageal junction. We noticed that there was no change in the trend for the proportion and frequency of SCC in both these sub-sites over 20 years. However, it is interesting to note that AC in the lower oesophagus without involving the gastro-oesophageal junction was present even in the early period of our study.

Our study has the limitations of a retrospective analysis and it does not give true incidence data. This is not a population based study, but based on data from a tertiary care centre. Difficulty in exactly determining the extent of neoplasms in some cases is a limitation our study. This might have led to false estimation of AC in gastro-oesophageal junction.

We conclude that the lower end of the oesophagus is the predominant site of oesophageal cancer in South India. Adenocarcinoma is the predominant histologic type of cancer in lower end lesions involving the the gastro-oesophageal junction and squamous cell carcinoma is the predominant histologic type in lower end neoplasms of the oesophagus not involving the gastro-oesophageal junction. Even though statistically not significant, lower end neoplasms involving the gastro-oesophageal junction especially AC has shown a consistent increase in frequency which requires further longitudinal studies. However, there was no change in trend of frequency and proportion of squamous cell carcinoma at these sub- sites over a twenty-year period.

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